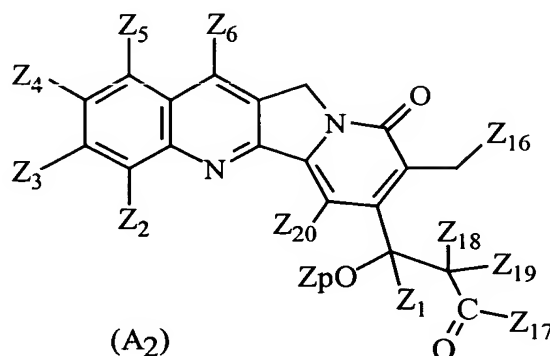
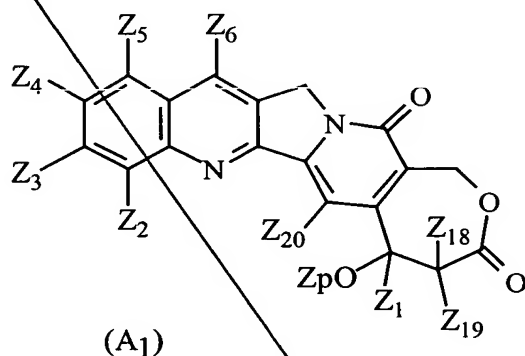


# CLAIMS

Amend.  
a<sup>2</sup>

1. Compounds of general formula (A<sub>1</sub>) or (A<sub>2</sub>)



in racemic or enantiomeric form or any combinations of these forms, in which

5 Z<sub>1</sub> represents a lower alkyl, a lower alkenyl, a lower alkynyl, a lower haloalkyl, a lower alkoxy lower alkyl or lower alkylthio lower alkyl;

Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub> and Z<sub>6</sub> represent, independently,

10 i) H, halo, lower haloalkyl, alkyl containing 1 to 12 carbon atoms optionally substituted by one or more halo radicals indentical or different, lower alkenyl, cycloalkyl, cycloalkyl lower alkyl, cyano, lower cyanoalkyl, nitro, lower nitroalkyl, amido, lower amidoalkyl, hydrazino, lower hydrazinoalkyl, azido, lower azidoalkyl, lower alkyl lower sulphonylalkyl,  $-(CH_2)_mNZ'_6Z'_7$ ,  $-(CH_2)_mOZ'_6$ ,  $-(CH_2)_mSZ'_6$ ,  $-(CH_2)_mCO_2Z'_6$ ,  $-(CH_2)_mNZ'_6C(O)Z_8$ ,  $-(CH_2)_mC(O)Z_8$ ,  $-(CH_2)_mOC(O)Z_8$ ,  $-O(CH_2)_mNZ'_6Z'_7$ ,  $-OC(O)NZ'_6Z'_7$ ,  $-OC(O)(CH_2)_mCO_2Z'_6$ ,  $-OSO_2Z_7$ ,  $-(CH_2)_mN(CH_3)(CH_2)_nNZ'_6Z'_7$ ,  $-(CH_2)_mOC(O)NZ'_6Z'_7$ ,  $-(CH_2)_mS(O)_qZ_{11}$ ,  $-(CH_2)_mP(O)Z_{12}Z_{13}$ ,  $-(CH_2)_2P(S)Z_{12}Z_{13}$ ,  $-(CH_2)_mSiZ'_{11}Z'_{12}Z'_{13}$ , or ii)  $-(CH_2)_n[N=X]$ ,  $-OC(O)[N=X]$ ,  $-(CH_2)_mOC(O)[N=X]$ , aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group or the heterocycle) or non substituted in which the substituent is a lower alkyl, lower arylalkyl, halo, hydroxy,  $-OCF_3$ , nitro, amino, lower alkylamino, di(lower alkyl)amino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl or iii) Z<sub>3</sub> and Z<sub>4</sub> or Z<sub>4</sub> and Z<sub>5</sub> form together a chain with 3 or 4 members in which the elements of the chain are selected from the group constituted by CH, CH<sub>2</sub>, O, S, N or NZ<sub>9</sub>;

15

20

25

contd.  
Q 2

- 5  $Z_6$  and  $Z'_7$  represents a lower alkyl radical optionally substituted by one or more halo radicals identical or different, or an aryl optionally substituted by one or more lower alkyl radicals identical or different ;
- 10  $Z_8$  represent, independently, i) H, a lower alkyl, lower hydroxyalkyl, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy lower alkyl, lower haloalkyl, or ii) aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group) or non substituted in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl ;
- 15  $Z_9$  represents i) H, a lower alkyl, lower hydroxyalkyl, amino, lower alkylamino, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy, lower alkoxy lower alkyl, lower haloalkyl, or ii) aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group) or non substituted, in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl;
- 20  $Z_{10}$  represents i) H, a lower alkyl, lower haloalkyl, or ii) aryl or lower arylalkyl, each substituted or non substituted in which the substituent is lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl;
- 25  $Z_{11}$  represents i) H, a lower alkyl, lower haloalkyl, lower alkoxy, or ii) aryl substituted (i.e. having one to four substituents on the aryl group) or non substituted in which the substituent is lower alkyl, lower haloalkyl, lower hydroxyalkyl or lower alkoxy lower alkyl;
- 30  $Z_{12}$  and  $Z_{13}$  represents a lower alkyl, aryl,  $-(CH_2)_mOZ_{14}$ ,  $-(CH_2)_mSZ_{14}$ ,  $-(CH_2)_2NZ_{14}Z_{15}$  or  $-(CH_2)_m[N=X]$ ;
- $Z'_{11}$ ,  $Z'_{12}$  and  $Z'_{13}$  represent, independently, H or a lower alkyl radical ;
- $Z_{14}$  and  $Z_{15}$  represent, independently, H, lower alkyl or aryl;
- 35  $Z_{16}$  represents H or  $-OZ_{21}$ ;
- $Z_{17}$  represents  $-OZ'_6$  or  $-NZ'_6Z'_7$  ;
- $Z_{18}$  and  $Z_{19}$  represent, independently, H, halo, lower alkyl, lower alkoxy or hydroxy;
- $Z_{20}$  represents H or halo;

10071046-020602

contd.  
a<sup>2</sup>

- ~~Z<sub>21</sub> represents H, a lower alkyl, -CHO or -C(O)(CH<sub>2</sub>)<sub>m</sub>CH<sub>3</sub>;~~  
~~Z<sub>p</sub> represents H or an easily cleavable group preferably chosen from the groups corresponding to the formula -C(O)-A-NZ<sub>22</sub>Z<sub>23</sub>, in which A represents a linear or branched alkylene radical optionally substituted by a radical chosen from the free, esterified or salified hydroxy, halogen, free, esterified or salified carboxy, amino, mono or dialkylamino radicals ;~~  
~~5        Z<sub>22</sub> and Z<sub>23</sub> represent, independently, H, a lower alkyl, lower hydroxyalkyl, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy lower alkyl, lower haloalkyl, or substituted or non substituted aryl or lower arylalkyl (i.e., substituted one to four times on the aryl group), in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl;~~  
~~10        m is an integer comprised between 0 and 6;~~  
~~n is 1 or 2; and~~  
~~q represents an integer from 0 to 2; and~~  
~~[N=X] represents a heterocyclic group with 4 to 7 members with the nitrogen atom which is a member of the heterocyclic ring, and X representing the chain necessary to complete said heterocyclic group and selected from the group constituted by O, S, CH<sub>2</sub>, CH, N, NZ<sub>9</sub> and C(O)Z<sub>10</sub> ;~~  
~~20~~

or pharmaceutically acceptable salts of thereof.

2. Compounds of general formula (A<sub>1</sub>) or (A<sub>2</sub>) as claimed in claim 1, in racemic or enantiomeric form or any combinations of these forms, characterized in that

- ~~25        Z<sub>1</sub> represents a lower alkyl, a lower alkenyl, a lower alkynyl, a lower haloalkyl, a lower alkoxy lower alkyl or lower alkylthio lower alkyl;~~  
~~Z<sub>2</sub> represents H, halo or -OSO<sub>2</sub>Z<sub>7</sub> ;~~  
~~Z<sub>3</sub>, Z<sub>4</sub> and Z<sub>5</sub> represent, independently, i) H, halo, lower haloalkyl, lower alkyl, lower alkenyl, cyano, lower cyanoalkyl, nitro, lower nitroalkyl, amido, lower amidoalkyl, hydrazino, lower hydrazinoalkyl, azido, lower azidoalkyl,~~  
~~30        -(CH<sub>2</sub>)<sub>m</sub>NZ'<sub>6</sub>Z'<sub>7</sub>, -(CH<sub>2</sub>)<sub>m</sub>OZ'<sub>6</sub>, -(CH<sub>2</sub>)<sub>m</sub>SZ'<sub>6</sub>, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>Z'<sub>6</sub>,~~  
~~-(CH<sub>2</sub>)<sub>m</sub>NZ'<sub>6</sub>C(O)Z<sub>8</sub>, -(CH<sub>2</sub>)<sub>m</sub>C(O)Z<sub>8</sub>, -(CH<sub>2</sub>)<sub>m</sub>OC(O)Z<sub>8</sub>,~~  
~~-O(CH<sub>2</sub>)<sub>m</sub>NZ'<sub>6</sub>Z'<sub>7</sub>, -OC(O)NZ'<sub>6</sub>Z'<sub>7</sub>, -OC(O)(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>Z'<sub>6</sub>, -OSO<sub>2</sub>Z<sub>7</sub> or~~  
~~35        ii) -(CH<sub>2</sub>)<sub>n</sub>[N=X], -OC(O)[N=X], -(CH<sub>2</sub>)<sub>m</sub>OC(O)[N=X] (in which [N=X], in this invention, represents a heterocyclic group with 4 to 7 members with the nitrogen atom N, which is a member of the heterocyclic group, and X represents the remaining members, which are~~

10071046-020602

contd.  
A 2

5

necessary to complete the heterocyclic group, selected from the group constituted by O, S, CH<sub>2</sub>, CH, N, NZ<sub>9</sub> and COZ<sub>10</sub>), aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group or the heterocycle) or non substituted in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl or iii) Z<sub>3</sub> and Z<sub>4</sub> or Z<sub>4</sub> and Z<sub>5</sub> form together a chain with 3 or 4 members in which the elements of the chain are selected from the group constituted by CH, CH<sub>2</sub>, O, S, N or NZ<sub>9</sub>;

10 Z<sub>6</sub>

represents i) H, halo, lower haloalkyl, alkyl containing 1 to 12 carbon atoms optionally substituted by one or more halo radicals identical or different, lower alkoxy, lower alkoxy lower alkyl, lower alkylthio lower alkyl, cycloalkyl, cycloalkyl lower alkyl, cyano, cyanoalkyl, lower alkyl lower sulphonylalkyl, lower hydroxyalkyl, nitro, -(CH<sub>2</sub>)<sub>m</sub>C(O)Z<sub>8</sub>, -(CH<sub>2</sub>)<sub>m</sub>NZ'<sub>6</sub>C(O)Z<sub>8</sub>, -(CH<sub>2</sub>)<sub>m</sub>NZ'<sub>6</sub>Z'<sub>7</sub>, -(CH<sub>2</sub>)<sub>m</sub>N(CH<sub>3</sub>)(CH<sub>2</sub>)<sub>n</sub>NZ'<sub>6</sub>Z'<sub>7</sub>, -(CH<sub>2</sub>)<sub>m</sub>OC(O)Z<sub>8</sub>, -(CH<sub>2</sub>)<sub>m</sub>OC(O)NZ'<sub>6</sub>Z'<sub>7</sub>, -(CH<sub>2</sub>)<sub>m</sub>S(O)<sub>q</sub>Z<sub>11</sub>, -(CH<sub>2</sub>)<sub>m</sub>P(O)Z<sub>12</sub>Z<sub>13</sub>, -(CH<sub>2</sub>)<sub>2</sub>P(S)Z<sub>12</sub>Z<sub>13</sub>, -(CH<sub>2</sub>)<sub>m</sub>SiZ'<sub>11</sub>Z'<sub>12</sub>Z'<sub>13</sub>; or ii) -(CH<sub>2</sub>)<sub>n</sub>[N=X], -OC(O)[N=X], -(CH<sub>2</sub>)<sub>m</sub>OC(O)[N=X], each substituted (i.e. substituted between once and four times on the heteroaryl group)

15

20

or non substituted in which the substituent is a lower alkyl, lower arylalkyl, halo, hydroxy, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl; or iii) aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group) or non substituted in which the substituent is a lower alkyl, halo, hydroxy, nitro, -OCF<sub>3</sub>, amino, lower alkylamino, di(lower alkyl)amino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl ;

Z<sub>7</sub>

represents a lower alkyl radical optionally substituted by one or more halo radicals identical or different, or an aryl optionally substituted by one or more lower alkyl radicals identical or different ;

30

Z'<sub>6</sub> and Z'<sub>7</sub>

represent, independently, i) H, a lower alkyl, lower hydroxyalkyl, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy lower alkyl, lower haloalkyl, or ii) aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group) or non substituted in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl ;

35

contd.  
a<sup>2</sup>

200020" 94012001

- 5  $Z_8$  represents i) H, a lower alkyl, lower hydroxyalkyl, amino, lower alkylamino, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy, lower alkoxy lower alkyl, lower haloalkyl, or ii) aryl or lower arylalkyl, each substituted (i.e. substituted between once and four times on the aryl group) or non substituted, in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl;
- 10  $Z_9$  represents i) H, a lower alkyl, lower haloalkyl, or ii) aryl or lower arylalkyl, each substituted or non substituted in which the substituent is lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl;
- 15  $Z_{10}$  represents i) H, a lower alkyl, lower haloalkyl, lower alkoxy, or ii) aryl substituted (i.e. having one to four substituents on the aryl group) or non substituted in which the substituent is lower alkyl, lower haloalkyl, lower hydroxyalkyl or lower alkoxy lower alkyl;
- $Z_{11}$  represents a lower alkyl, aryl,  $-(CH_2)_mOZ_{14}$ ,  $-(CH_2)_mSZ_{14}$ ,  $-(CH_2)_2NZ_{14}Z_{15}$  or  $-(CH_2)_m[N=X]$ ;
- 20  $Z_{12}$  and  $Z_{13}$  represent, independently, a lower alkyl, aryl, lower alkoxy, aryloxy or amino;
- $Z'_{11}$ ,  $Z'_{12}$  and  $Z'_{13}$  represent, independently, H or a lower alkyl radical ;
- $Z_{14}$  and  $Z_{15}$  represent, independently, H, lower alkyl or aryl;
- $Z_{16}$  represents H or  $-OZ_{21}$ ;
- $Z_{17}$  represents  $-OZ'_6$  or  $-NZ'_6Z'_7$  ;
- 25  $Z_{18}$  and  $Z_{19}$  represent, independently, H, halo, lower alkyl, lower alkoxy or hydroxy;
- $Z_{20}$  represents H or halo;
- $Z_{21}$  represents H, a lower alkyl,  $-CHO$  or  $-C(O)(CH_2)_mCH_3$ ;
- $Z_p$  represents H or an easily cleavable group preferably chosen from the groups corresponding to the formula  $-C(O)-A-NZ_{22}Z_{23}$ , in which A represents a linear or branched alkylene radical optionally substituted by a radical chosen from the free, esterified or salified hydroxy, halogen, free, esterified or salified carboxy, amino, mono or dialkylamino radicals ;
- 30  $Z_{22}$  and  $Z_{23}$  represent, independently, H, a lower alkyl, lower hydroxyalkyl, lower alkyl lower aminoalkyl, lower aminoalkyl, cycloalkyl, cycloalkyl lower alkyl, lower alkenyl, lower alkoxy lower alkyl, lower haloalkyl, or substituted or non substituted aryl or lower arylalkyl (i.e., substituted

contd.  
Q2

- one to four times on the aryl group), in which the substituent is a lower alkyl, halo, nitro, amino, lower alkylamino, lower haloalkyl, lower hydroxyalkyl, lower alkoxy or lower alkoxy lower alkyl;
- m is an integer comprised between 0 and 6;
- 5 n is 1 or 2; and
- q represents an integer from 0 to 2; and
- [N=X] represents a heterocyclic group with 4 to 7 members with the nitrogen atom which is a member of the heterocyclic ring, and X representing the chain necessary to complete said heterocyclic group and selected
- 10 from the group constituted by O, S, CH<sub>2</sub>, CH, N, NZ<sub>9</sub> and COZ<sub>10</sub> ;
- or pharmaceutically acceptable salts of thereof.
3. Compounds as claimed in claim 1 or 2, characterized in that Z<sub>2</sub> represents H or halo ; or pharmaceutically acceptable salts of thereof.
4. Compounds as claimed in claim 1 or 2, characterized in that Z<sub>3</sub> represents halo ; or pharmaceutically acceptable salts of thereof.
- 15 5. Compounds as claimed in any of claims 1 to 4, characterized in that
- Z<sub>1</sub> represents a lower alkyl ;
- Z<sub>2</sub> represents H or halo ;
- 20 Z<sub>3</sub>, Z<sub>4</sub> and Z<sub>5</sub> represent, independently, i) H, halo, lower alkyl, -(CH<sub>2</sub>)<sub>m</sub>NZ'<sub>6</sub>Z'<sub>7</sub>, -(CH<sub>2</sub>)<sub>m</sub>OZ'<sub>6</sub>, -OSO<sub>2</sub>Z'<sub>7</sub> or ii) -(CH<sub>2</sub>)<sub>n</sub>[N=X] or iii) Z<sub>3</sub> and Z<sub>4</sub> or Z<sub>4</sub> and Z<sub>5</sub> form together a chain with 3 or 4 members in which the elements of the chain are selected from the group constituted by CH, CH<sub>2</sub>, O, S, N or NZ<sub>9</sub>;
- 25 Z<sub>6</sub> represents i) H, halo, alkyl containing 1 to 12 carbon atoms optionally substituted by one or more halo radicals identical or different, lower alkoxy lower alkyl, cycloalkyl, cycloalkyl lower alkyl, lower hydroxyalkyl, -(CH<sub>2</sub>)<sub>m</sub>NZ'<sub>6</sub>Z'<sub>7</sub>, -(CH<sub>2</sub>)<sub>m</sub>SiZ'<sub>11</sub>Z'<sub>12</sub>Z'<sub>13</sub> ; or ii) -(CH<sub>2</sub>)<sub>n</sub>[N=X] substituted or non substituted in which the substituent is a lower alkyl or lower arylalkyl or iii) aryl or lower arylalkyl, each
- 30 substituted or non substituted in which the substituent is a lower alkyl, halo, -OCF<sub>3</sub>, di(lower alkyl)amino or lower haloalkyl ;
- Z<sub>7</sub> represents a lower alkyl radical optionally substituted by one or more halo radicals identical or different ;
- Z'<sub>6</sub> and Z'<sub>7</sub> represent, independently, i) H, a lower alkyl, or ii) lower arylalkyl ;
- 35 Z<sub>9</sub> represents a lower alkyl or lower arylalkyl ;
- Z'<sub>11</sub>, Z'<sub>12</sub> and Z'<sub>13</sub> represent, independently, a lower alkyl radical ;

10071046-020602

5

10

20

7. Compounds as claimed in any of claims 1 to 6, characterized in that Z<sub>1</sub> represents ethyl ; or pharmaceutically acceptable salts of thereof.

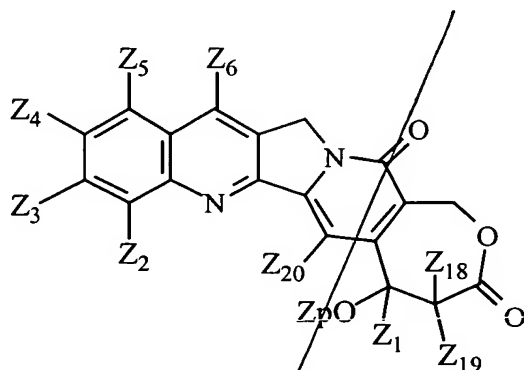
25

9. Compounds as claimed in claim 1 or 2, characterized in that Z<sub>p</sub> represents H ; or pharmaceutically acceptable salts of thereof.

10. Compounds as claimed in claim 1 or 2, characterized in that they correspond to the ~~formula (A1)~~

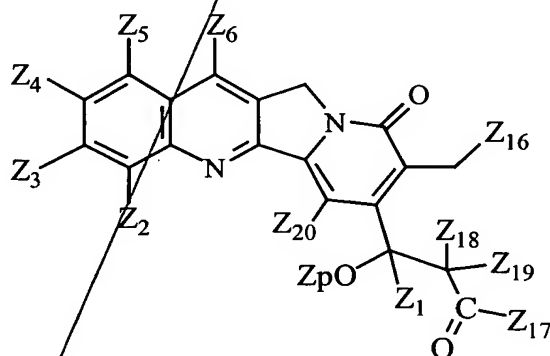
Figure 1 consists of 12 histograms arranged horizontally, labeled  $k=0$  through  $k=11$ . Each histogram shows the frequency of the number of non-zero elements in the vector  $x_k$ . The x-axis for each histogram is 'Number of non-zero elements' with ticks at 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10. The y-axis is 'Frequency' with ticks at 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10. The distributions are roughly bell-shaped and centered around 5-6 non-zero elements.

contd  
a<sup>2</sup>



wherein  $Z_1$ ,  $Z_2$ ,  $Z_3$ ,  $Z_4$ ,  $Z_5$ ,  $Z_6$ ,  $Z_{18}$ ,  $Z_{19}$ ,  $Z_{20}$  and  $Z_p$  are as defined in claim 1 ; or pharmaceutically acceptable salts of thereof.

- 5 11. Compounds as claimed in claim 1 or 2, characterized in that they correspond to the formula (A2)



wherein  $Z_1$ ,  $Z_2$ ,  $Z_3$ ,  $Z_4$ ,  $Z_5$ ,  $Z_6$ ,  $Z_{16}$ ,  $Z_{17}$ ,  $Z_{18}$ ,  $Z_{19}$ ,  $Z_{20}$  and  $Z_p$  are as defined in claim 1 ; or pharmaceutically acceptable salts of thereof.

- 10 12. Compounds as claimed in claim 1 or 2, characterized in that  $Z_6$  represents  $-(CH_2)_mSiZ'_{11}Z'_{12}Z'_{13}$  ; or pharmaceutically acceptable salts of thereof.

13. Compounds as claimed in claim 12, characterized in that they correspond to the following formula :

(5*R*)-5-ethyl-9,10-difluoro-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino[3',4':6,7]indolizino [1,2-*b*] quinoline-3,15-dione ;

- 15 (5*R*)-5-ethyl-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino [3',4':6,7]indolizino [1,2-*b*] quinoline-3,15-dione ;

- 20 14. Compounds as claimed in claim 1 or 2, characterized in that  $Z_2$  represents H or halo,  $Z_3$  represents halo,  $Z_4$  represents H, halo or lower alkyl,  $Z_5$  represents H or halo, and  $Z_6$  represents H, lower alkyl or  $-(CH_2)_n[N=X]$  substituted in which the substituent is a lower alkyl ; or pharmaceutically acceptable salts of thereof.

20071046-020602



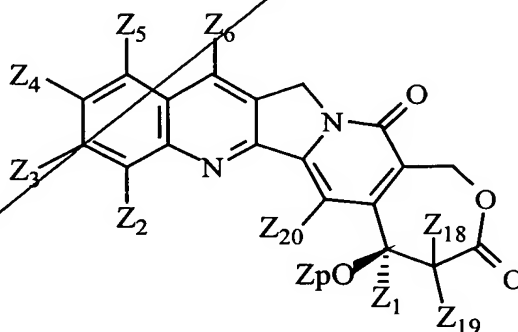
contd.  
A<sup>2</sup>

15. Compounds as claimed in claim 14, characterized in that they correspond to the following formula :

(5*R*)-5-ethyl-9,11-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino [3',4':6,7] indolizino [1,2-*b*] quinoline-3,15-dione ;

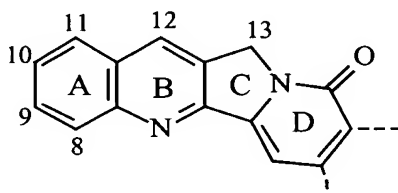
- 5 (5*R*)-5-ethyl-9,11-difluoro-5-hydroxy-12-propyl-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino [3',4':6,7] indolizino [1,2-*b*] quinoline-3,15-dione ; or pharmaceutically acceptable salts of thereof.

16. Compounds as claimed in claim 1 or 2, characterized in that they correspond to the formula

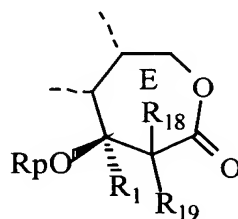


10 wherein Z<sub>1</sub>, Z<sub>2</sub>, Z<sub>3</sub>, Z<sub>4</sub>, Z<sub>5</sub>, Z<sub>6</sub>, Z<sub>18</sub>, Z<sub>19</sub>, Z<sub>20</sub> and Z<sub>p</sub> are as defined in claim 1 ; or pharmaceutically acceptable salts of thereof.

17. A method of treating cancer in warm-blooded animals comprising administering to warm-blooded animals in need thereof a camptothecin analog characterized in that  
15 said analog is a [A,B,C,D,E] pentacyclic compound, the cycles [A,B,C,D]



comprising any substitution on the various sites available for substitution(s), and the [E] cycle being a 7-ring member  $\beta$ -hydroxy lactone ring of the formula



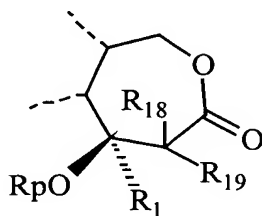
wherein  $R_1$  is selected from the group consisting of alkyl of 1 to 6 carbon atoms, alkenyl and alkynyl of 2 to 6 carbon atoms, haloalkyl of 1 to 6 carbon atoms, alkoxyalkyl of 2 to 12 carbon atoms and alkylthioalkyl of 2 to 12 carbon atoms,  $R_p$  is hydrogen or an easily cleavable group,  $R_{18}$  and  $R_{19}$  are individually selected from the group consisting of hydrogen, halogen, OH and alkyl and alkoxy of 1 to 6 carbon atoms and its non-toxic, pharmaceutically acceptable salts.

18. A method of treating cancer according to claim 17, the cycles [A,B,C,D] comprising any substitution on the sites 8, 9, 10, 11, 12 or 13.

19. A method of treating cancer according to claim 17, the cycles [A,B,C,D] comprising any substitution on the sites 8, 9, 10, 11 or 12.

20. A method of treating cancer according to claim 17, the cycles [A,B,C,D] comprising any substitution on the sites 9, 10, 11 or 12.

21. A method of treating cancer in warm-blooded animals comprising administering to warm-blooded animals in need thereof a camptothecin having 5 rings with a 7-ring member  $\beta$ -hydroxy lactone ring of the formula



wherein  $R_1$  is selected from the group consisting of alkyl of 1 to 6 carbon atoms, alkenyl and alkynyl of 2 to 6 carbon atoms, haloalkyl of 1 to 6 carbon atoms, alkoxyalkyl of 2 to 12 carbon atoms and alkylthioalkyl of 2 to 12 carbon atoms,  $R_p$  is hydrogen or an easily cleavable group,  $R_{18}$  and  $R_{19}$  are individually selected from the group consisting of hydrogen, halogen, OH and alkyl and alkoxy of 1 to 6 carbon atoms and its non-toxic, pharmaceutically acceptable salts.

22. A method of treating cancer as claimed in claim 17 or 21, characterized in that cancer is selected from the group consisting of leukemia, colon cancer, lung cancer, prostate cancer, breast cancer, melanoma, ovarian cancer and gastric cancer.

23. A method of treating cancer as claimed in claim 22, characterized in that cancer is selected from the group consisting of leukemia, colon cancer, lung cancer, prostate cancer and breast cancer.

24. A method as claimed in any of claims 17 to 23 characterized in that  $R_{18}$  and  $R_{19}$  are hydrogen.

25. A method as claimed in any of claims 17 to 24 characterized in that  $R_p$  is hydrogen.

26. A method as claimed in any of claims 17 to 25 characterized in that  $R_1$  is ethyl.

27. A method as claimed in any of claims 17 to 26 characterized in that camptothecin analog is selected from :

(5R)-5-ethyl-9,10-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7] indolizino [1,2-b] quinoline-3,15-dione ;

(5R)-1-[9-chloro-5-ethyl-5-hydroxy-10-methyl-3,15-dioxo-4,5,13,15-tetrahydro 1H,3H-oxepino [3',4':6,7] indolizino [1,2-b] quinolin-12-yl-methyl]-4-methyl-hexahydropyridium chloride ;

(5R)-5-ethyl-9,11-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7] indolizino [1,2-b] quinoline-3,15-dione ;

(5R)-5-ethyl-9,11-difluoro-5-hydroxy-12-propyl-4,5,13,15-tetrahydro-1H,3H-oxepino [3',4':6,7] indolizino [1,2-b] quinoline-3,15-dione ; or its pharmaceutically acceptable salts thereof.

amen.  
a3

10071045-0006002